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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,986	07/01/2002	Seishi Nagamori	56972 (71526)	2684
21874	7590	03/06/2008		
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EXAMINER				
HORNING, MICHELLE S				
ART UNIT		PAPER NUMBER		
1648				
MAIL DATE		DELIVERY MODE		
03/06/2008		PAPER		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

**Office Action Summary****Application No.**

10/049,986

**Applicant(s)**

NAGAMORI, SEISHI

**Examiner**

MICHELLE HORNING

**Art Unit**

1648

**Period for Reply** -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 04 December 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 21-29 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 21-29 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/CDC)
- 4) ☐ Interview Summary (PTO-413)
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_
- Paper No(s)/Mail Date \_\_\_\_\_

### **DETAILED ACTION**

This office action is responsive to communication filed 12/04/2007. The status of the claims is as follows: claims 21-29 are pending and under current examination and claims 1-20 have been cancelled.

The following rejection has been withdrawn:

1. 35 USC 112, 1<sup>st</sup> paragraph (Enablement).

Applicants' present other prior art teachings which demonstrate cell lines other than the FLC4 cell line that successfully support HCV expression, including the HepG2 cells and Huh7 cells as taught by Seipp et al (see Remarks, page 4). This has been found persuasive and this rejection has been withdrawn.

### ***Claim Rejections - 35 USC § 103-MAINTAINED***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

**Claims 21-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawada et al (1998) and Aoki et al (1998).**

Briefly, Kawada et al teach a radial flow bioreactor coupled with a highly functional liver cell line. The authors show that use of this invention resulted in cells with both their natural morphology and function. Additionally, the continuous flow of media generates a beneficial concentration of oxygen and nutrients while preventing excessive shear stresses or build up of waste products. The authors teach that the *in vivo* state

can be achieved. Lastly, the authors point out that conventional culture systems lead to 1. short culture lifespan and insufficient cellular function and productivity due to poor culture environment, 2. insufficient cell density, and 3. difficulty to scale-up culture processes.

Separately, Aoki et al teach that the FLC4 cell line successfully supports efficient growth of HCV and this cell line exhibits very high reporter gene expression with pT7HCVLuc in comparison to the low success rates of various other cell lines.

In conclusion, the ordinary artisan would have combined a successful cell culture system to achieve optimal condition for the cells (Kawada et al) and would have particularly used a cell line known to successfully express HCV (Aoki et al).

In response, Applicants provide nebulous arguments. More specifically, each reference fails to provide all of the claimed limitations (see Remarks, pages 5-6). Additionally, Applicants provide the following recitation: "one skilled in the art would not expect that the propagation of HCV in the radial flow bioreactor under the continuous stream of a liquid culture medium would give  $10^5$  of HCV stably for 100 days" (see Remarks, page 5).

The arguments are considered but not found persuasive. First, the Examiner will not accept the invitation to read the following limitation into the claims: "would give  $10^5$  of HCV stably for 100 days". Secondly, Applicants have failed to properly address the motivation of combining the two prior art teachings. More specifically, as stated on page 6 of the previous office action and above, Kawada et al provide three clear reasons why the disclosed culture system is more successful than that of a conventional system and

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Aoki et al disclose the success of FL4C cells in HCV growth compared to that of other cell lines. Of note, Applicants provide the following recitation in response to the rejection under 35 USC 112, 1<sup>st</sup> paragraph: "HCV actually proliferates in living human liver. The skilled artisan would therefore readily understand that HCV could proliferate in any human hepatocyte..." (see Remarks, page 4-5). With this in mind, the skill artisan would also provide a cell culture system for the hepatocytes which would provide optimal conditions, as taught by Kawada et al; see discussion above.

### ***Conclusion***

NO CLAIM IS ALLOWED.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **MICHELLE HORNING** whose telephone number is

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(571)272-9036. The examiner can normally be reached on Monday-Friday 8:00-5:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campbell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michelle Horning/  
Examiner, Art Unit 1648

/Bruce Campbell/  
Supervisory Patent Examiner, Art Unit 1648